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Therapeutic angiogenesis. A single intraarterial bolus of vascular endothelial growth factor augments revascularization in a rabbit ischemic hind limb model.

Takeshita S, Zheng LP, Brogi E, Kearney M, Pu LQ, Bunting S, F N, Symes JF, Isner JM.

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Vascular endothelial growth factor (VEGF) is a heparin-binding, endothelial cell-specific mitogen. Previous studies have suggested that VEGF is a regulator of naturally occurring physiologic and pathologic angiogenesis. In this study we investigated the hypothesis that the angiogenic potential of VEGF is sufficient to constitute a therapeutic effect. The soluble 165-amino acid isoform of VEGF was administered as a single intra-arterial bolus to the internal iliac artery of rabbits in which the ipsilateral femoral artery was excised to induce severe unilateral hind limb ischemia. Doses of 500–1,000 micrograms produced statistically significant augmentation of collateral vessel development by angiography as well as the number of capillaries on histology; consequent amelioration of the hemodynamic deficit in the ischemic limb was significantly greater in animals receiving VEGF than in nontreated controls (calf blood pressure ratio, 0.75 ± 0.14 vs. 0.55 ± 0.19 , $P < 0.05$). Serial angiograms disclosed progressive linear extension of the collateral artery of origin (stem artery) to the distal point of parent vessel (reentry artery) reconstitution in seven of the VEGF-treated animals. These findings establish proof of principle for the concept that the angiogenic activity of VEGF is sufficiently potent to achieve therapeutic benefit. Such a strategy might ultimately be applicable to patients with severe limb ischemia secondary to arterial occlusive disease.

PMID: 7509344 [PubMed – indexed for MEDLINE]

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Route of administration

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In pharmacology and toxicology, a **route of administration** is the path by which a drug, fluid, poison or other substance is brought into contact with the body.

(Note: in toxicology, "exposition" may often be a more appropriate term, however "administration" can be used for deliberate substance use.)

Obviously, a substance must be transported from the site of entry to the part of the body where its action is desired to take place (unless this is on the body surface). However, using the body's transport mechanisms for this purpose can be far from trivial. The pharmacokinetic properties of a drug (that is, those related to processes of uptake, distribution, and elimination) are critically influenced by the route of administration.

Classification

Routes of administration can broadly be divided into:

- **topical**: local effect, substance is applied directly where its action is desired
- **enteral**: desired effect is systemic (non-local), substance is given via the digestive tract
- **parenteral**: desired effect is systemic, substance is given by other routes than the digestive tract

The following is a list of some common routes of administration.

Topical:

- intracutaneous (injection into the skin), e.g. allergy testing
- epicutaneous (application onto the skin), e.g. allergy testing, topical local anesthesia
- inhalative, e.g. asthma medications

- enema, e.g. contrast media for imaging of the bowel

Enteral:

- by mouth, many drugs as tablets, capsules, or drops
- by gastric feeding tube, duodenal feeding tube, or gastrostomy, many drugs and enteral nutrition
- rectally, various drugs

Parentral by injection or infusion:

- intravenous (into a vein), e.g. many drugs, total parenteral nutrition
- intraarterial (into an artery), e.g. vasodilator drugs in atherosclerosis
- intramuscular (into a muscle), e.g. vaccines
- subcutaneous (under the skin), e.g. insulin

Parentral (other than injection or infusion):

- transdermal (diffusion through the intact skin), e.g. transdermal opioid patches in pain therapy
- transmucosal (diffusion through a mucous membrane), e.g. cocaine snorting, sublingual nitroglycerine
- inhalative, e.g. inhalation anesthetics

Other:

- intraperitoneal (infusion or injection into the peritoneal cavity), e.g. peritoneal dialysis
- epidural or peridural (injection or infusion into the epidural space), e.g. epidural anesthesia
- intrathecal (injection or infusion into the cerebrospinal fluid), e.g. antibiotics, spinal anesthesia

Some routes can be used for topical as well as systemic purposes, depending on the circumstances. For example, inhalation of asthma drugs is targeted at the airways (topical effect), whereas inhalation of volatile anesthetics is targeted at the brain (systemic effect).

On the other hand, identical drugs can produce different results depending on the route of administration. For example, some drugs are not significantly absorbed into the bloodstream from the gastrointestinal tract and their action after enteral administration is therefore different from that after **parenteral** administration. This can be illustrated by the action of naloxone, an antagonist of opiates such as morphine. Naloxone counteracts opiate action in the central nervous system when given intravenously and is therefore used in the treatment of opiate overdose. The same drug, when swallowed, acts exclusively on the bowels; it is here used to treat constipation under opiate pain therapy and does not affect the pain-reducing effect of the opiate.

Uses

Enteral routes are generally the most convenient for the patient, as no punctures or sterile procedures are necessary. Enteral medications are therefore often preferred in the treatment of chronic disease. However, some drugs can not be used enterally because their absorption in the digestive tract is low or unpredictable. Transdermal administration is a comfortable alternative; there are, however, only few drug preparations suitable for transdermal administration.

In acute situations, in emergency medicine and intensive care medicine, drugs are most often given intravenously. This is the most reliable route, as in acutely ill patients the absorption of substances from the tissues and from the digestive tract can often be unpredictable due to altered blood flow or bowel motility.

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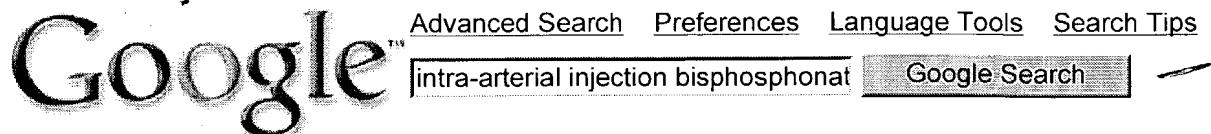
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